**Remarks**

The following is a response to the Office Action mailed June 16, 2005.

Upon entry of the amendment, claims 1-3, 5-9, 11-12, 14-16, 18-19, 25-34, 36-37 and 39-46 will be pending. Claims 1 and 25 have been amended. Claims 10 and 35 have been canceled without prejudice. Claims 4, 13, 17, 20-24, 38 and 47-72 were previously withdrawn.

Amendments to the claims are fully supported in the specification and claims as filed, and therefore do not add new matter nor raise new issues.

Accordingly, entry of the amendment and withdrawal of the rejections is respectfully requested.

## I. Rejections under 35 U.S.C. §112, First Paragraph (written description)

Claims 1-3, 5-12, 14-16, 18-19, 25-37 and 39-46 are rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

According to Office Action, there is no written description for the genus term, "kallikrein-like peptidase"; and that a review of the specification indicates only one kallikrein-like peptidase species, i.e. kallikrein (paragraph bridging pages 2 and 3 of the Office Action).

Applicants submit that claim terms are presumed to have the ordinary and customary meanings attributed to them by those of ordinary skill in the art. *Sunrace Roots Enter. Co. v. SRAM Corp.*, 336 F.3d 1298, 1302, 67 USPQ2d 1438, 1441 (Fed. Cir. 2003); *Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1298 67 USPQ2d 1132, 1136 (Fed. Cir. 2003)("In the absence of an express intent to impart a novel meaning to the claim terms, the words are presumed to take on the ordinary and customary meanings attributed to them by those of ordinary skill in the art."). It is the use of the words in the context of the written description and customarily by those skilled in the relevant art that accurately reflects both the "ordinary" and the

"customary" meaning of the terms in the claims. *Ferguson Beauregard/Logic Controls v. Mega Systems*, 350 F.3d 1327, 1338, 69 USPQ2d 1001, 1009 (Fed. Cir. 2003).

Hence, in the absence of an express intent to impart a novel meaning to the claim terms (e.g., "kallikrein-like peptidase"), the words are presumed to take on the *ordinary and customary* meanings attributed to them *by those of ordinary skill in the art phrase*. See *Intuitive Surgical, Inc., supra.* The ordinary and customary meaning of "kallikrein-like peptidase" can be found in the art, for example, see Exhibit A (Lilja, H. 1985 "A kallikrein-like serine protease in prostatic fluid cleaves the predominant seminal vesical protein," *J. Clin. Invest.* 76(5):1899-903). The art defines "kallikrein-like peptidases" structurally (e.g., NH2-terminal amino acid sequences) and/or functionally (e.g., hydrolyzing or cleaving various substrates at the arginine (R) site). See Exhibit A.

Functional activity of "kallikrein-like peptidase" is described in the application as filed. For example, AGLTR-pNA, S2288, and S2302 are detection reagents or substrates which *if* in the presence of a "kallikrein-like peptidase" are hydrolyzed. Hence, one skilled in the art will understand that a "kallikrein-like peptidase" functions by hydrolyzing or cleaving a substrate, for example, the arginine (R) in substrates AGLTR-pNA, S2288, and S2302. Cleavage of these substrates releases the yellow-colored pNA which can be monitored at a visible wavelength of 405 nm; see page 28, paragraph **[0089]**). Applicants submit that this functional criteria of the claimed "kallikrein-like peptidase" adequately describes the entire genus, as *all* "kallikrein-like peptidase" enzymes share this common trait, including plasma kallikrein.

The ordinary and customary usage of "kallikrein-like peptidase" or "kallikrein-like activity" is also demonstrated in Hayashi, which discloses that "C1s failed to convert the AGLTR-pNA or the kallikrein substrate S2302, while LTR plasma and plasma kallikrein converted both (see Abstract). Hayashi "concluded that the proteinase detected in these LTR plasma were neither C1s, but was primarily *kallikrein-like activity* associated with the α2-M (see Abstract)."

The ordinary and customary usage of "kallikrein-like peptidase" is also described in Exhibit A (Lilja), which discloses that a "kallikrein-like peptidase" of about 33 kDa has structural (e.g., NH2-terminal sequence strongly suggests that it belongs to the family of glandular kallikreins) and functional (e.g., hydrolyzed arginine containing substrates) characteristics of a "kallikrein-like peptidase" (see Exhibit A).

Thus, for all the foregoing reasons, the phrase "kallikrein-like peptidase" is understood by one skilled in the art and its use in the claimed invention is sufficiently described.

Accordingly, withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph is respectfully requested.

**II. Rejections under 35 U.S.C. §102(a) and (b)**

Claims 1-3, 5-12, 14, 16 and 18-19 are rejected under 35 U.S.C. § 102(a) and (b) as being allegedly unpatentable because they are anticipated by Hayashi et a. (August 5-9, 2000; hereinafter, "Hayashi"). Applicants respectfully traverse all these rejections.

Under 35 U.S.C. § 102, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference (emphasis added)." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 0987). Further , "[t]he identical invention [should it be taught in the cited reference] must be shown in as complete detail as is contained in the ...claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

The Declarations of Dr. Tony E. Hugli and Dr. Craig Jackson are enclosed and state that: 1) Hayashi has a publication date of August 5-9, 2000 and was not mailed prior to the date of the Symposium, or August 5, 2000. Since August 5, 2000 is within the one year of the filing of the above-identified application (August 2, 2001) a rejection under 35 U.S.C. § 102(b) is improper; and the rejection is a 35 U.S.C. § 102(a) reference; and 2) Tony E. Hugli, a co-applicant of the above-identified application, and a co-author of the Hayashi 35 U.S.C. § 102(a), in the reference is describing work originating from, and obtained from, him.

Therefore, Applicant's Declaration rebuts a 35 U.S.C. § 102(a) *prima facie* case.

Accordingly, withdrawal of the rejection of claims 1-3, 5-12, 14, 16 and 18-19 under 35 U.S.C. § 102(a) and (b) is respectfully requested.

## V. Rejections under 35 U.S.C. §103

Claims 1, 15, 25-37, and 39-46 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Hayashi in view of Pfeifer et al. (2000; hereinafter, "Pfeifer"). Applicants respectfully traverse all these rejections.

According to the Office Action, Hayashi discloses liver damage by detecting levels of pNA, and Pfeifer discloses that measuring C3a and C4a levels is a means of monitoring liver damage over a period of time, and together Hayashi and Pfeifer allegedly make obvious the claimed invention.

Claims 1 and 25 have been amended and claims 10 and 35 have been canceled, because the subject matter in these claims has been incorporated into claims 1 and 25.

Applicants submit that if Hayashi and Pfeifer were modified such that they disclose the claimed invention, the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

Pfeifer discloses that "unique patterns of C3a and C4a levels, together with organ-specific parameters, appear to *correlate* with a number of pathological conditions or clinical events...[and that] profiles and patterns of C3a/C4a levels can be used as reliable monitor of rejection episodes, immune status and/or viral infections in ...transplant patients (p. 173, col. 1, last paragraph)." The purpose of Pfeifer is that patterns of C3a/C4a are indicative of acute rejection and secondary response following primary CMV infection (see p. 171, col. 2, second

paragraph). These, results are also described in the instant application (see page 43, paragraph **[0118]**).

In contrast, the claimed subject matter is based on the finding that elevated enzyme levels correlate with hepatitis infection (claims 1 and 35), but that there was no correlation between the peptidase activity and either organ rejection or CMV infection (see p. 39, paragraph **[0110]** of the specification; see page 43, paragraph **[0118]**)." Thus, modifying Pfeifer by combining it with Hayashi would "render [Pfeifer] being modified unsatisfactory for its intended purpose," because in affect using a kallikrein-like peptidase detecting reagent is not indicative of acute rejection or CMV infection.

Also, Hayashi in view of Pfeifer, do not teach or suggest the all the claim limitations. As discussed above, the combination of Hayashi and Pfeifer does not teach or suggest that the kallikrein-like peptidase activity is indicative of liver damage caused by hepatitis.

Thus, for all the foregoing reasons, Hayashi and Pfeifer cannot make obvious the claimed invention.

Accordingly, withdrawal of the rejection of claims 1, 15, 25-37, and 39-46 under 35 U.S.C. § 103(a) is respectfully requested.

## Conclusion

In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to this application.

Applicants do not believe any other fees are due in connection with this submission, however if any other fees are due, please charge any fees, or make any credits, to Deposit Account No. 07-1896.

Respectfully submitted,

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1: J Clin Invest. 1985 Nov;76(5):1899-903.

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# A kallikrein-like serine protease in prostatic fluid cleaves the predominant seminal vesicle protein.

Lilja H.

A 33-kD glycoprotein, known as the "prostate-specific antigen," was purified to homogeneity from human seminal plasma. The prostatic protein was identified as a serine protease, and its NH2-terminal sequence strongly suggests that it belongs to the family of glandular kallikreins. The structural protein of human seminal coagulum, the predominant protein in seminal vesicle secretion, was rapidly cleaved by the prostatic enzyme, which suggests that this seminal vesicle protein may serve as the physiological substrate for the protease. The prostatic enzyme hydrolyzed arginine- and lysine-containing substrates with a distinct preference for the former. All synthetic substrates tested were poor substrates for the enzyme. Synthetic Factor XIa substrate (pyro-glutamyl-prolyl-arginine-p-nitroanilide), and the synthetic kallikrein substrate (H-D-prolyl-phenylalanyl-arginine-p-nitroanilide) were hydrolyzed with maximum specific activities at 23 degrees C of 79 and 34 nmol/min per mg and Km values of 1.0 and 0.45 mM, respectively. Synthetic substrates for plasmin, chymotrypsin, and elastase were either not hydrolyzed by the enzyme at all, or only hydrolyzed very slowly.

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